REMARKS

Claims 1-28 remain pending in the application. No amendments have been made herein.

The Examiner has leveled a restriction requirement. In response, I hereby elect, with traverse, Group I, claims 1-6, 8-13, 15-20 and 22-27, directed to methods of treatment wherein **beta interferon**, the active agent, is administered starting at about the 11th day or later after spinal cord injury.

In a December 22, 2006 telephone discussion, my representative, Dr. Richard Sterner, presented reasons to the Examiner why the present restriction of subject matter is inappropriate. The remarks below reiterate the points made during the discussion and provide additional details.

The times of treatment are not "mutually exclusive" as explained below.

The examiner states that the times of administration of beta-interferon are mutually exclusive; however, this is not the case. Administration at day 11 or later (e.g., claim 6) literally encompasses administration at the 4th week or later (e.g., claim 7). Put another way, although present claim 7 depends from claim 5, claim 7 could just as easily have been written to depend from claim 6.

The onset of chronic inflammation in response to spinal cord injury is on day 11 postinjury and it occurs at the lesion site proper, at the primary impact area. This is the first wave which leads to a massive tissue decay at the lesion site.

There is a secondary onset of chronic inflammation which is triggered in the intact tissue at the margin of the lesion site; this is a secondary (ripple wave) which penetrates and spreads into the intact undamaged cord tissue. This secondary onset of chronic inflammation within the intact normal tissue occurs at about the 4th week postinjury. This secondary wave leads to a secondary tissue decay, primarily to robust demyelination. It persists and constantly penetrates into the intact undamaged spared tissue.

If one treats with beta-interferon at day 11 postinjury, the onset of chronic inflammation is prevented; the primary wave is stopped and obviously there is no secondary wave. However, if one misses the primary timing, the secondary timing for preventing the penetration of chronic inflammation into the spared tissue would be at the 4th week postinjury. It is important to

understand that whether one begins treatment as early as the 11th day or waits until the 4th week or later, one is treating the same problem, namely, chronic inflammation.

There are no differing chances for success by the treatment as explained below.

The Examiner further contends that the methods of restriction Groups I and II are distinct because they have differing chances of success. However, as explained during the December 22, 2006 telephone discussion and as set forth below, this is not the case.

The focus of the present invention is chronic inflammation which leads to tissue decay.

There is only one invention and it is targeted to stop/prevent with beta-interferon the chronic inflammation that is triggered in response to injury in the spinal cord and leads to tissue decay. There is a primary tissue damage at the impact area; and there is a delayed secondary tissue damage at the intact tissue, adjacent to the impact area, which is triggered at a later time in response to the primary tissue damage.

There is a "good" curative/healing inflammation and a "bad" pathologic/ damaging inflammation, i.e., the chronic inflammation. The "good" inflammation goes up in response to insult, removing the unwanted dead cells and pathogens etc. and then it goes down and vanishes by day 5-6 after the insult. The "bad" chronic inflammation is an inflammation which cannot be downregulated and persists forever, such as in autoimmune diseases. In the spinal cord the chronic inflammation is triggered at about day 11 after injury.

The "maximal inflammation" the Examiner refers to on p.3 l. 1 of the Office Action appears to be the "good" curative inflammation which peaks in the spinal cord on day 3-4 after injury. This is not what we are talking about. We are talking about the chronic inflammation.

The following are citations from the Patent Application, as originally filed, denoted by paragraph number:

"[0033] This invention is intended to treat chronic human spinal cord injury. The invention is intended to adapt an already established clinical procedure for the treatment of the neurodegenerative disease multiple sclerosis (MS) — the use of beta interferon — to treat chronic human spinal cord injury. ... Since the underlying event leading to chronic inflammation in chronic SCI has now been found to be identical to the event in MS, the present

invention is directed to beta-interferon treatment to prevent chronic inflammation and its devastating consequences in chronic SCI.

[008] The working hypothesis that led to this invention is that the breakdown of the blood-cord barrier following SCI leads to chronic inflammation which is the culprit in SCI pathology. ... It is assumed that the loss of function in the intact/spared fibers is due to the secondary damage caused by the chronic inflammation which is triggered at about the 3rd week after spinal cord injury.

[0016] Our preliminary data, in a rat spinal cord contusion injury model, show that chronic inflammation at the lesion site is triggered, at the molecular level, only by the end of the 2nd and/or 3rd week after injury. Our data show that following injury the expression of VCAM-1 on cord endothelial cells starts to increase above background levels only by the end of the 2nd week and/or 3rd week and that it becomes expansive throughout the lesion site by the 4th week postinjury [Burrows, et al., (2002) Program No. 133.10., *2002 Abstract Viewer/Itinerary Planner.* Washington, DC: Society for Neuroscience, Online]. Based on our observations, it is anticipated that beta interferon would suppress the pathologic enhanced expression of VCAM-1 following spinal cord injury in the same manner it does in experimental models of MS. It is anticipated that beta interferon would gain access to the lesion site via the leaky BBB and would exert its physiological function, inhibiting thereby the chronic inflammation and demyelination and thus leading to rescue of neurologic function of the spared, uninjured spinal cord tissue including the spared brain-cord fiber tracts.

[0035] The analysis suggests chronic inflammation associated with SCI is an ongoing process at the site of lesion that can be stopped/attenuated by treatment with beta interferon. Preferably, the treatment should start at about the 11th day after injury when the decay is triggered, but it can be applied months or even years after injury to rescue the spared tissue from further degeneration.

[0042] ... Altogether, it appears that the switch from repair to decay occurs during day 10-14 after injury."

Application/Control No.: 10/693042
Art Unit: 1647

It must be concluded from the disclosure of the specification that claims 1-28 comprise a single invention in accordance with U.S. restriction practice. Further consideration of the application with all of the originally filed claims is respectfully requested.

Dated: January 8, 2007

Respectfully submitted,

Nurit Kalderon

Nurit Kalderon, Ph.D.
P (212) 564-9498
F (212) 486-9105

REMARKS

Claims 1-28 remain pending in the application. No amendments have been made herein.

The Examiner has leveled a restriction requirement. In response, I hereby elect, with traverse, Group I, claims 1-6, 8-13, 15-20 and 22-27, directed to methods of treatment wherein **beta interferon**, the active agent, is administered starting at about the 11th day or later after spinal cord injury.

In a December 22, 2006 telephone discussion, my representative, Dr. Richard Sterner, presented reasons to the Examiner why the present restriction of subject matter is inappropriate. The remarks below reiterate the points made during the discussion and provide additional details.

The times of treatment are not "mutually exclusive" as explained below.

The examiner states that the times of administration of beta-interferon are mutually exclusive; however, this is not the case. Administration at day 11 or later (e.g., claim 6) literally encompasses administration at the 4th week or later (e.g., claim 7). Put another way, although present claim 7 depends from claim 5, claim 7 could just as easily have been written to depend from claim 6.

The onset of chronic inflammation in response to spinal cord injury is on day 11 postinjury and it occurs at the lesion site proper, at the primary impact area. This is the first wave which leads to a massive tissue decay at the lesion site.

There is a secondary onset of chronic inflammation which is triggered in the intact tissue at the margin of the lesion site; this is a secondary (ripple wave) which penetrates and spreads into the intact undamaged cord tissue. This secondary onset of chronic inflammation within the intact normal tissue occurs at about the 4th week postinjury. This secondary wave leads to a secondary tissue decay, primarily to robust demyelination. It persists and constantly penetrates into the intact undamaged spared tissue.

If one treats with beta-interferon at day 11 postinjury, the onset of chronic inflammation is prevented; the primary wave is stopped and obviously there is no secondary wave. However, if one misses the primary timing, the secondary timing for preventing the penetration of chronic inflammation into the spared tissue would be at the 4th week postinjury. It is important to

understand that whether one begins treatment as early as the 11th day or waits until the 4th week or later, one is treating the same problem, namely, chronic inflammation.

There are no differing chances for success by the treatment as explained below.

The Examiner further contends that the methods of restriction Groups I and II are distinct because they have differing chances of success. However, as explained during the December 22, 2006 telephone discussion and as set forth below, this is not the case.

The focus of the present invention is chronic inflammation which leads to tissue decay.

There is only one invention and it is targeted to stop/prevent with beta-interferon the chronic inflammation that is triggered in response to injury in the spinal cord and leads to tissue decay. There is a primary tissue damage at the impact area; and there is a delayed secondary tissue damage at the intact tissue, adjacent to the impact area, which is triggered at a later time in response to the primary tissue damage.

There is a "good" curative/healing inflammation and a "bad" pathologic/ damaging inflammation, i.e., the chronic inflammation. The "good" inflammation goes up in response to insult, removing the unwanted dead cells and pathogens etc. and then it goes down and vanishes by day 5-6 after the insult. The "bad" chronic inflammation is an inflammation which cannot be downregulated and persists forever, such as in autoimmune diseases. In the spinal cord the chronic inflammation is triggered at about day 11 after injury.

The "maximal inflammation" the Examiner refers to on p.3 l. 1 of the Office Action appears to be the "good" curative inflammation which peaks in the spinal cord on day 3-4 after injury. This is not what we are talking about. We are talking about the chronic inflammation.

The following are citations from the Patent Application, as originally filed, denoted by paragraph number:

"**[0033]** This invention is intended to treat chronic human spinal cord injury. The invention is intended to adapt an already established clinical procedure for the treatment of the neurodegenerative disease multiple sclerosis (MS) — the use of beta interferon — to treat chronic human spinal cord injury. ... Since the underlying event leading to chronic inflammation in chronic SCI has now been found to be identical to the event in MS, the present

invention is directed to beta-interferon treatment to prevent chronic inflammation and its devastating consequences in chronic SCI.

[008] The working hypothesis that led to this invention is that the breakdown of the blood-cord barrier following SCI leads to chronic inflammation which is the culprit in SCI pathology. ... It is assumed that the loss of function in the intact/spared fibers is due to the secondary damage caused by the chronic inflammation which is triggered at about the 3rd week after spinal cord injury.

[0016] Our preliminary data, in a rat spinal cord contusion injury model, show that chronic inflammation at the lesion site is triggered, at the molecular level, only by the end of the 2nd and/or 3rd week after injury. Our data show that following injury the expression of VCAM-1 on cord endothelial cells starts to increase above background levels only by the end of the 2nd week and/or 3rd week and that it becomes expansive throughout the lesion site by the 4th week postinjury [Burrows, et al., (2002). Program No. 133.10., *2002 Abstract Viewer/Itinerary Planner*. Washington, DC: Society for Neuroscience, Online]. Based on our observations, it is anticipated that beta interferon would suppress the pathologic enhanced expression of VCAM-1 following spinal cord injury in the same manner it does in experimental models of MS. It is anticipated that beta interferon would gain access to the lesion site via the leaky BBB and would exert its physiological function, inhibiting thereby the chronic inflammation and demyelination and thus leading to rescue of neurologic function of the spared, uninjured spinal cord tissue including the spared brain-cord fiber tracts.

[0035] The analysis suggests chronic inflammation associated with SCI is an ongoing process at the site of lesion that can be stopped/attenuated by treatment with beta interferon. Preferably, the treatment should start at about the 11th day after injury when the decay is triggered, but it can be applied months or even years after injury to rescue the spared tissue from further degeneration.

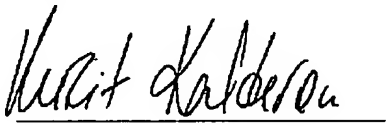
[0042] ... Altogether, it appears that the switch from repair to decay occurs during day 10-14 after injury."

Application/Control No.: 10/693042
Art Unit: 1647

It must be concluded from the disclosure of the specification that claims 1-28 comprise a single invention in accordance with U.S. restriction practice. Further consideration of the application with all of the originally filed claims is respectfully requested.

Dated: January 8, 2007

Respectfully submitted,



Nurit Kalderon, Ph.D.
P (212) 564-9498
F (212) 486-9105